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Leptin is Not Associate with Maternal Fat Mass on the Third Trimester of Pregnancy

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Abstract

Leptin was initial known as adipocyte product link to the obese gene. Pregnancy is a physiologic leptin resistance state. The placenta is reported to synthesize and release leptin too. This study is to observe the association between maternal serum leptin with maternal body fat mass on the third trimester of pregnancy. Leptin was measured by ELISA from the serum of maternal on median pregnancy age 30 weeks. Maternal body fat mass was measured by bioelectrical impedance analyzing (BIA) methods.

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The mean of maternal fat mass is, M= 20,1 kg, SD= 5,2, minimum 10,6 kg and maximum 35,3 kg. Leptin, M= 46,9 µgr/L, SD= 32,6, minimum 5,8 µgr/L and maximum 146,7 µgr/L. Univariate analysis showed, in third trimester of pregnancy, maternal serum leptin could not predict the maternal fat mass appropriately, SS 14,007, MS 4,67, F (3, 66) = 0,17, p 0,92, partial η^2 0,01. This current study shows, leptin level is higher during the third trimester of pregnancy and not associate with maternal fat mass. In the third trimester of pregnancy, maternal serum leptin could not predict the maternal fat mass precisely.

Keywords: pregnancy; leptin; fat mass; placenta.

1. Introduction

Pregnancy is a unique model to investigate the metabolism of adipose tissue. During pregnancy, the maternal metabolic hormones have fluctuated specifically to adapt the physiologic changing of hemostasis of maternal energy. These hormonal changes, including, hyperinsulinemia, hyperleptinemia and increased levels of cortisol, estrogen, progesterone and human placental lactogen (hPL) [1]. In pregnancy, energy homeostasis shifts towards the storage of fat which is characterized by hyperphagia and decreased of energy expenditure [2, 3, 4, 5, 6].

Leptin is a peptide synthesized and secreted by white adiposity. This peptide, which has a structure resembling the cytokines, identified first by Zhang and his colleagues in 1994 [7, 8]. In energy homeostasis, leptin to function as the main messenger status of energy in fat depot. On the individual in norm leptinemia, activated of hypothalamus nucleus by leptin will induce a number of cascades across those nucleuses and produce the anorexigenic behavior, decrease in appetite, and an increase in energy expenditures [9, 10]. In pregnancy, energy homeostasis shifts towards the increasing of the fat depot which was marked with hyperphagia as well as the decrease of energy expenditure [2, 3, 4, 5, 6]. The buildup of fat depot happens physiologically as a guarantee of the continuity of supply of energy to the fetus [2, 3, 6]. This physiological process allegedly linked to adaptive physiological leptin resistance in pregnancy [2, 4, 5, 6, 11]. Leptin was mainly produced in adipose tissue but also is expressed in various tissues including placenta, ovarian, mammary epithelium, bone marrow and lymphoid tissue [12,13]. Placental development is optimizing in the third trimester, and this study is to observe the association between leptin with maternal fat mass in the third trimester of pregnancy.

2. Materials and Method

2.1. Study Design and Samples

This current study is part of authors longitudinal study about energy hemostasis during pregnancy. Inclusion criteria are pregnant women on pregnancy age $\leq$ 28 weeks. Maternal who is diagnosed type 2 diabetes mellitus, thyroid dysfunction, kidney dysfunction, twins' pregnancy and eclampsia, are not included in this study. Samples which analyzed in this current study are 70 pregnant women on 3rd visit, the median pregnancy age is 30 weeks. This study was done in primary health care center in Bahu, Tuminting, Ranotana, Ranomuut and Wawonasa, all were located in Manado, the capital city of Province of North Sulawesi, Indonesia. Ethical clearance was evaluated and approved by the Ethical Committee of RSUP Prof. Dr. R. D. Kandou, Manado, no.

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2.2. Variables

The dependent variable is maternal fat mass in median pregnancy age 30 weeks. Maternal fat mass is measured by bioelectrical impedance analysis (BIA) methods using OMRON HBF-358-BW. The independent variable is maternal serum leptin. The serum is obtained from blood sample which is collected simultaneously with the anthropometric measurement. Leptin is analyzed by ELISA methods using the kit from Quantikine® ELISA, Human leptin Immunoassay, Catalog Number DLP00, R&D Systems. The analyses of leptin were conducted at NHCR Laboratories, Academic Hospital of Faculty of Medicine, University of Hasanuddin, Makassar, Indonesia.

2.3. Statistical Analysis

Statistical analysis to predict the association of maternal serum leptin and fat mass is conducted using general linear model (GLM) univariate. Leptin as predictor was categorized base on Tukey's Hinges percentiles (< 25, >25-39, >39-59, > 59 µgr/L). All statistical analysis was conducted using IBM SPSS Statistics version 22.

3. Results

The majority of participants were 18 – 35 years old. About 17% of maternal have the pre-pregnancy BMI < 18,5 kg/m^2 and 39% were overweight/obese. More than 50% have body height $\leq$ 155 cm. The base characteristic of samples is present in Table 1.

Table 1: Base Characteristics of Samples

		Sample (n=70)	%
Age (yrs.')			
	>18	2	3
	18-25	25	36
	26-35	37	53
	>35	6	9
Body height (cm)			
	$\leq$155	36	51
	>155	34	49
Pre-pregnancy BMI (Kg/m^2)			
	<18,5	12	17
	18,5-22,9	31	44
	$\geq$23,0	27	39
Parity			
	1	24	34
	2	28	40
	3	12	17
	>3	6	9

The mean of maternal fat mass is, M= 20,1 kg, SD= 5,2, minimum 10,6 kg and maximum 35,3 kg. Leptin, M= 46,9 µgr/L, SD= 32,6, minimum 5,8 µgr/L and maximum 146,7 µgr/L. The mean of fat mass on leptin ≤ 25 µgr/L is 19,5 kg, not so difference with maternal who has serum leptin > 59 µgr/L. Figure 1.

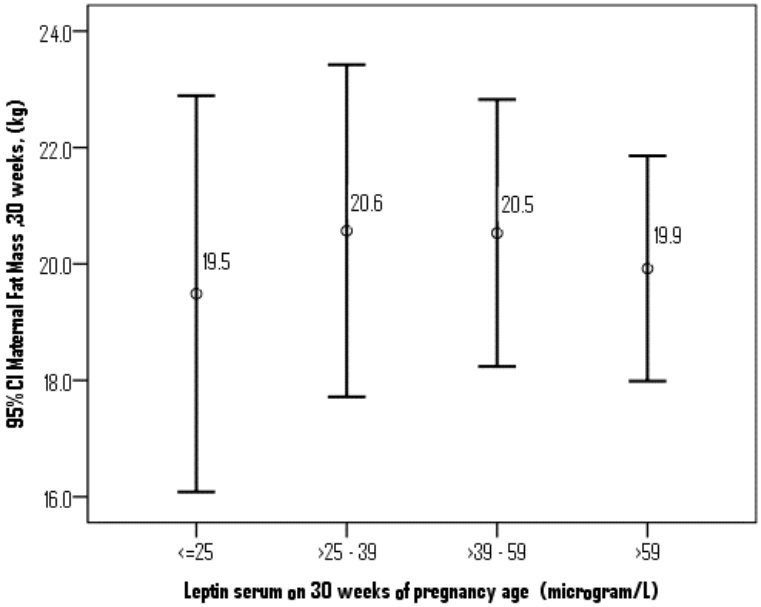

Figure 1: Mean ((95%CI) of Maternal Fat Mass According to Concentration of Leptin

Univariate analysis showed, in third trimester of pregnancy, the maternal serum leptin could not predict the maternal fat mass precisely, SS 14,007, MS 4,67, F (3, 66) = 0,17, p 0,92, partial η^2 0,01. Maternal fat mass on leptin serum < 25 µgr/L was lower than on > 59 µgr/L, but not significantly different, Table 2.

Table 2: Association of leptin serum and maternal fat mass

Leptin (µgr/L)	B	95% CI		*p*	Partial η^2
		Lower	Upper		
Intercept	19,9	17,4	22,4	*0,00*	0,79
<=25 to > 59	-0,4	-4,0	3,2	*0,81*	0,00
>25-39 to > 59	0,6	-2,8	4,1	*0,71*	0,00
>39-59 to > 59	0,6	-3,0	4,3	*0,74*	0,00

4. Discussion

Numerous studies confirm that pregnancy is characterized by hyperleptinemia [2, 3, 6]. Leptin levels in pregnant women are higher compared to non-pregnant women [14, 15]. Mean maternal leptin levels in this

study is, M = 46.9 μgr / L, SD = 32.6, much higher than the average of leptin in women of childbearing age who are not pregnant, ranged < 15 ng / ml, as reported by Ajala and his colleagues 2013 [15]. The increasing of leptin had already detected on the gestational age of 15 weeks and reached the peak at week 35, both in pregnant women with pre-pregnant BMI less, normal or more [14].

In the mammals' system of hemostasis of energy, leptin is a determinant messenger from that carries information about the status of stored energy (fat mass depot) to the arcuate nucleus in the hypothalamus [7, 8, 16]. Activation of the receptor ObRb by leptin in the membrane of neurons anorexigenic nucleus arcuate (POMC and CART) will induce the anorexigenic process and simultaneously inhibits the activity of neurons orexigenic (NPY and AgRP). So, we could assume, in appropriate condition, the leptin levels in range, the receptors function properly and the post-receptor activities work as it should, then there will be not a storage of fatty tissue that exceeds the body's needs. In pregnancy, there is an increase of maternal fat depots allegedly linked to adaptive, physiologically, leptin resistance. The mechanism of this adaptive physiologic leptin resistance during pregnancy has not been comprehensively understood.

Our current study showed that in the third trimester of pregnancy, leptin levels increase higher than maternal fat mass. Our results support the theory that placenta synthesizes and release leptin into the maternal circulation. Not many studies have studied the specific role of leptin during pregnancy. Placenta synthesizes and secretes leptin; leptin levels are high during pregnancy. This suggests that leptin in high amounts is needed during pregnancy. The role of leptin that occurs simultaneously to the balance of energy hemostasis, the reproductive system, and the immune system reflects the close interconnection between these three systems, which play an important role in the survival of a species, including humans [17, 18, 19, 20, 21, 22, 23]. The process of pregnancy requires adequate of energy, as an immune adaptation. Based on our current study results and many reported previous studies, we propose an assumption that leptin plays an integrative role both as messenger and regulator in the activities and interrelated adaptability of these three systems. We need some specific studies to unclose the suggestive mechanisms.

5. Conclusions

Leptin is higher in the third trimester of pregnancy. This higher level of leptin is not associate with maternal fat mass.

Conflict of Interest and Funding Disclosure

This work was supported by grants from Danone Institute Indonesia. The author declares, no conflict of interest of the funder with this study since preparation, doing and finalization.

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